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## THE COMMON COLD\*

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DISCUSSION by Francis Scott Smyth, M. D., San Francisco; George Piness, M. D., Los Angeles; William J. Kerr, M. D., San Francisco.

ONE approaches a discussion of this subject with a great deal of trepidation, for various reasons. First, because the splendid little book "Our Common Enemy: Colds," by the editors of "Fortune in Consultation with Eminent Physicians" (Robert M. McBride and Company, New York, Third Edition, 1934), has already cleared up a world of misinformation. In a most readable style, it presents a controversial subject and discusses the means to prevent and cure a cold. Vaccination receives benevolent sanction, ultraviolet rays and chlorin are treated with justified skepticism, while changes in diet are critically analyzed. Secondly, it is impossible for one mere mortal to review the rapidly increasing and scattered literature on the subject; and, thirdly, an epidemiologist is obviously not qualified to condense in a short communication the most important facts which may serve as guides for future researches. However, a humble attempt is herewith made.

### ACUTE RESPIRATORY DISEASES A LARGE FACTOR IN MORBIDITY AND MORTALITY RATES

No one will deny that the acute respiratory diseases assume a most important position in the morbidity and mortality rates of any civilized community. This is particularly true since medical science has so far failed to contribute an effective method either of prophylaxis or cure. Although of worldwide distribution and common occurrence, the common cold has only in recent epochs attracted attention. Consequently, the information as to the actual prevalence in different parts of the world, and at different times, is quite meager. It is admitted, and in part substantiated by observations on selected groups, that the tendency for recurrent attacks—on the average two per person per year

in a temperate climate—induce, in the aggregate, a tremendous loss in working time and efficiency of a population. Statistical data are difficult to collect on account of the inherent uncertainty of distinguishing between the common cold, a mild attack of influenza, a sinusitis or an allergic rhinitis. By common agreement, a mild respiratory catarrh is reported as a cold, while a more severe attack with fever is called influenza. Yet, an epidemic of a severe respiratory infection is quite generally designated as influenza. The relationship of pandemic influenza to annual or inter-epidemic influenza is by no means clear, and must by necessity encourage confusion. Various irritants, such as dust, chemical fumes, smoke, pollens, etc., can cause an acute catarrhal condition of the nose. This type of "cold" is, as a rule, described as an allergic, vasomotor rhinitis or perennial hay fever. A great deal of detective work is necessary properly to diagnose and identify these conditions. Such a state of affairs complicates the collection of accurate epidemiologic data. One is justified, therefore, in making the bold statement that the "common cold" recognized in medical practice is certainly not a definite single disease. Experience has taught that the most frequently observed colds are contagious, and thus differ from the allergic catarrhs which are nonorganismal and noninfectious.

### RECENT EVIDENCE CONCERNING THE INFECTIOUSNESS OF "COLDS"

What recent evidence has been presented to prove the infectiousness of a cold? Heinbecker and Irvine-Jones (1929), during a trip up the west coast of Greenland, noted that in certain of the settlements every native was the victim of an acute respiratory tract infection, while in others no evidence of such infection was present. Careful surveys revealed that, in the former, some contact had invariably been made with the outside world prior to their coming, while in the latter group, within from forty-eight to seventy-two hours after their arrival, all the natives developed acute respiratory disturbances with sneezing, coughing and spitting. Farther north, among the polar Eskimos, where it was certain that no outside contact had been made during that year, there

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was never the slightest evidence of acute respiratory tract disease at the time of the arrival of the expedition, but within seventy-two hours nearly every Eskimo of the settlement developed such a malady. Epidemiologic investigations by Burky and Smillie (1929) in southern Alabama and in Labrador, and by Milani and Smillie (1931) on the Island of St. John (U. S. Virgin Islands, West Indies), indicate that the colds with the customary nasopharyngeal picture are infectious, and spread by direct contact with an incubation period of one to three days. However, the latter investigators present evidence which strongly incriminates environmental influences—for example, a drop in atmospheric temperature—as predisposing, if not inciting, factors in the causation of acute colds.

In a series of illuminating experiments on human volunteers housed during the period of observation in a room in which the temperature and humidity were carefully controlled, Kerr and Lagen failed to secure evidence that the common cold is transmissible. Neither intimate contact with individuals suffering from a cold, nor the direct instillation of his unfiltered nasal secretions, conveyed the disease from man to man. These and other observations should caution us not to accept unconditionally the infectiousness of the common cold. A study of the predisposing factors along physiological lines is obviously indicated.

A chance observation by Long, Bliss and Carpenter, in connection with their studies on respiratory infections in chimpanzees, indicates that the common cold is transmissible during the incubation period. Under carefully controlled conditions, two of nine apes developed typical colds following contact with an attendant who was late in the incubation stage of a common cold. These reports, together with those of Jordan, Norton and Sharp, and Winholt and Jordan and previous observations, amply confirm the general epidemiologic evidence that one group of "colds" is contagious or infectious.

#### POSSIBLE NATURE OF THE INFECTIVE AGENT

However, concerning the nature of the infective agent, no agreement has as yet been reached. Two possibilities are mentioned, and evidence in favor of *bacterial* and *virus* colds has been presented. It appears profitable to investigate the intimate relationship between pathogens, whether bacteria or viruses, and the upper respiratory tract symptoms.

1. *Bacterial Colds*.—After the discoveries by Pasteur and Koch, attention was turned to the bacteriologic investigation of the diseases of the respiratory tract including the common cold. The earlier workers believed that colds were caused by various kinds of bacteria such as the Pfeiffer's bacillus, pneumococci, streptococci, micrococcus catarrhalis, Friedländer's bacillus, etc. The controversies as to the cause of pandemic influenza led to the belief that the true disease incitant responsible for this scourge was some invisible filter-passer, and that B. influenza was merely a secondary invader to the virus infection. This idea was soon accepted for the common cold, and it has been the leading conception in the current medical

literature. In fact, views which are not in harmony with this conception on the etiology remain submerged. In recent years, however, a number of careful studies have been published. They cast doubt on the virus theory of colds. In fact, they definitely prove that bacteria, in particular B. influenzae and pneumococci, are the primary causes of colds. Independently Webster and Hughes, Webster and Clow, Parks and others in America, and Thomson and Thomson, and Hoyle in England, after careful research extending over several years, both during health and during colds, conclude that these microorganisms are the primary causes of attacks of colds. Persons free of pneumococci, B. influenzae and streptococcus hemolyticus were found, in general, free of coryza, sore throat, influenzal and sinus attacks. During or following an attack, the persons become carriers of the organisms for a longer or shorter period. Boyle found that the attacks were associated with a high incidence of B. influenzae (71 per cent), pneumococci (67 per cent) and short-chained streptococci (48 per cent). Particularly instructive are, however, the lessons to be learned from these careful studies, that it is almost impossible to incriminate any particular organism as a cause of colds until the bacterial flora of a given number of individuals has been thoroughly studied for a period of years, not only during the periods of colds but also during health. It is equally important to stress the fact that the recent studies on a limited number of individuals contradict the mass observations on a large number of persons whose bacterial flora was determined during health and during colds by Noble and Brainard, Shibley, Dochez and Mills, Burky and Smillie, Blackburn, Boston and others. Since they failed to find any material difference in the bacterial flora of the respiratory tract during health or during colds, they either state definitely or infer that the bacteria play the part of secondary invaders. Yet, the most ardent believer in the filterable virus as the sole cause of the highly contagious cold admits that bacterial infections, due to hemolytic streptococci, produce a type of pharyngitis difficult to distinguish from the common forms of respiratory infection.

#### A CLASSIFICATION OF BACTERIAL COLDS

Parks has shown that in an institution of children, the boys living on one side of the street developed colds and pneumonias, while the girls, who were housed in a separate place, remained free from the disease. A filterable virus would have spread to the other street, but the causative pneumococci did not do so. For the sake of future inquiries, the clinical bacteriologist may classify the bacterial colds in their order of importance as follows:

(a) *Pneumococcal Colds*.—These are due to different types of pneumococci; clinically, this type of cold induces a purulent rhinitis frequently complicated with sinusitis, otitis media and pneumonia.

(b) *Pfeiffer's Bacillus Colds*.—These are caused by several varieties of this organism. Frequently responsible for a tracheitis and other complications.

(c) *Micrococcus Catarrhalis* and *Streptococcus Colds*.—The frequency and the significance of this type is not definitely established. The etiologic rôle of the green streptococci thus far presented is not convincing. It is claimed that these organisms are capable of causing colds of the copious watery type. Aside from the organisms mentioned, cases have been reported in which the *B. bronchisepticus* and various other bacteria assumed a significant numerical predominance.

2. *Virus Colds*.—Following the early experiments by Kruse (1914), Foster (1916 and 1917), Dodd (1917), Schmidt (1920), it became generally recognized that certain forms of coryza may be caused by agents present in the Berkefeld N filtrates of nasal washings obtained from patients with acute nasal catarrhs. Subsequently, Olitzsky and McCartney, while studying *B. pneumosintes*, encountered in the filtered nasal secretion from fresh cases of common colds in man an incitant which produced a definite coryza in some of the volunteers. However, the evidence was by no means convincing, since no controls for the irritative properties of the filtrates had been included. Little progress was made until Dochez, Shibley and Mills accidentally discovered that the "common cold" of man, or something closely resembling it from a clinical standpoint, apparently occurs among anthropoid apes. Thus, they attempted in 1929 to transmit "colds" from human beings to apes by the intranasal injection of filtered nasal washings from human patients. The transmission of colds was successful in about half of the inoculated animals. Very great difficulty was encountered in securing adequate controls on account of the prevalence of colds among the human beings which furnished the nasal washings. They repeated the same experiments during the summer (June and July). In no case did the filtrates from healthy subjects, during this period, give rise to catarrhal or other lesions in the apes inoculated with them. In subsequent experimental series on young chimpanzees, Dochez, Mills and Kneeland reproduced with regularity, by intranasal inoculations with bacteria free Seitz filtrates of nasopharyngeal washings from individuals with acute colds (within twenty-four to forty-eight hours), a definite respiratory disease consisting of sneezing, coughing, nasal obstruction, and mucoid or mucopurulent nasal discharge. The manifestations persisted for five days to two weeks. These experimental infections are communicable by contact to healthy chimpanzees placed in the same cage, and may be passed in series from animal to animal over a period of years. It is of interest that, coincident with the symptoms, various pathogenic organisms, influenza bacillus, hemolytic streptococci, formerly inconspicuous, develop in great numbers and spread over the mucous membranes. In fact, acutely-ill apes may convey these organisms to cage mates readily, while carriers rarely transfer bacteria by contact in the absence of an acute respiratory disease. Experimental transmission of colds on human volunteers revealed the same cycle of events as seen in the chimpanzees. The intranasal instillation of bacteria free filtrates from individuals suffering from acute colds resulted

after an incubation time of about twenty-four hours in a typical cold lasting from one to two weeks. Subsequent experiments indicated that the virus of the common cold survives for a considerable length of time after removal from the human pharynx, and that it reproduces itself in vitro when cultivated in the Maitland medium. In a more recent series Dochez succeeded in the cultivation of the virus directly from the nasopharyngeal washings obtained from a patient within twenty-four hours of the onset of a typical acute cold. The culture was passed through seventeen generations, and successfully infected one of three human volunteers.

Long, Doull, Bourn and McComb (1931) experimented along similar lines and succeeded in transmitting the common cold to human subjects by nasal instillations of nasopharyngeal washings obtained from patients suffering from the natural infection. Altogether, twenty inoculations were made from nine subjects with natural colds into nineteen volunteers. Eleven of these tests were successful in setting up colds. The incubation period was twenty to seventy hours; no cold developed after three days. In contrast to the observations of Dochez, these investigators failed to find striking differences between the bacterial flora of the nasopharynx studied during the period of initial quarantine and the period of experimental infection.

A third group of workers (Powell and Clowes, 1931) record a series of experiments carried out on human volunteers with a culture of "common cold" virus that had been carried through thirty-one generations in chick embryo tissue culture medium. Of thirty-two persons injected with the virus culture twenty-two developed colds.

#### CRITICISMS OF THE EXPERIMENTS

All these experiments have been criticized on the basis that the irritative, perhaps allergic properties of the filtrates were not properly controlled. This is true, since in one experiment a volunteer received an active culture heated for half an hour at 80 degrees centigrade; there appeared symptoms of upper respiratory irritation which, however, lasted only less than twenty-four hours. Doubtless, future experimenters must take these facts into consideration. Another criticism, voiced even more generally, objects to the relegation of the pneumococci, *B. influenzae* and streptococci to the status of secondary invaders, and the desire to make the etiology of the "common cold" a very simple process. That it is in all probability a complex process is indicated by the observations on animals.

Recent researches into the nature of a disease—swine influenza—resembling the common cold of man have shown that a hemophilic bacillus joins a filterable virus in helping to produce the respiratory disease. Variations in the invasiveness of the bacillus may profoundly modify the clinical course of the disease.

Even if it is recognized that this and other animal respiratory infections are dissimilar to the human cold, Th. Smith (1931) is doubtless cor-

rect when he makes the significant statement: "All species of animals have their respiratory diseases; and it would seem that if this enormous material, involving a variety of hosts and a still greater variety of microorganisms, could be brought together by some master mind synthetically inclined, the cause of human respiratory affection would literally drop into our laps."

The possible existence of filter-passing forms of bacteria must not be overlooked. It is indeed difficult to predict the influence of these newer discoveries on the bacteriology of the respiratory tract. Finally, it must be remembered also that many kinds of bacteria and viruses induce an inflammatory catarrh of the mucous membrane of the intestinal tract. Analogous conditions doubtless operate in the respiratory tract; and although one cannot overlook the important researches of Dochez and others, it is advisable to await further evidence, particularly concerning the mutual relationship of bacteria and viruses in the causation of respiratory disease.

#### THE "SOIL" OF THE "COLD"

In the etiology of the common cold, the "soil" is just as important as the seed. Future investigations must carefully consider the biochemistry of the blood and the secretions of the mucous membrane. By far, the greatest amount of research has been bacteriological, but the physiology and biochemistry of the patients liable to colds have been neglected. Some individuals have an inborn susceptibility to colds even though they have no nasal defects or late foci of infections. Moreover, an unusual susceptibility towards certain types of bacteria may be noted.

One would like to know more concerning the influence of chilling of the body surface on the ciliary mechanism and the mucous membrane of the respiratory tract, rendering it more susceptible to attack by microorganisms. Statistical, as well as experimental proof clearly show that chilling is a very important predisposing cause. Cold weather increases the chance of infection and, in a community the incidence of colds rises promptly after a sudden cold spell of weather.

Many other factors, including gastric upsets, are doubtless of importance. Poorly ventilated rooms increase the chances of droplet infection; fatigue reduces the general resistance, and anatomical and physiological defects impede the natural self-cleansing action of the nose, and create areas of stagnation well suited for localized microbial growth. The influence of diets and, in particular, vitamins, is by no means clear. Apparently, an abundance of the antirachitic vitamin does not increase the immunity to respiratory infections. There is no evidence that respiratory infections are due to deficiencies in vitamin A. Lack of vitamin C, on the other hand, induces a heightened local susceptibility with marked general loss of resistance.

While common colds are never fatal, the complications and sequelae cause great misery and far-reaching permanent damage. It is unnecessary to stress the disastrous effects of sinusitis, otitis

media, mastoiditis, pneumonia, endocarditis, etc. Why certain epidemics of colds give rise to a much higher percentage of these complications than others, is not known.

#### PREVENTION OF COLDS

The prevention of colds is quite generally directed towards the avoiding of the infection and in guarding against the predisposing causes. The modern conceptions of contact infection have encouraged general cleanliness and hygiene. If carried out faithfully by keeping a patient with a cold in bed and in isolation, this course of action will not only cure the cold but prevent it from spreading to others. This is the only advice which is scientifically justified. Since colds are certainly not definite single diseases, preventive vaccination remains an uncertain procedure. On the other hand, the curative treatment with autogenous vaccine preparations may be beneficial, although it may not be specific. Particularly, the local application of vaccine to the nasal cavities, to the throat and sinuses deserves further consideration.

Hooper Foundation for Medical Research.

#### DISCUSSION

FRANCIS SCOTT SMYTH, M.D. (University of California Hospital, San Francisco).—Doctor Meyer's discussion of the common cold is excellent. He points with sober consideration to the multiplicity of factors, bacteriological and clinical, which make any single theory untenable. At the present time "the 'common cold,' as recognized in medical practice, is not a definite single disease."

Pediatricians often observe the increased incidence of colds in school children previously carefully sheltered in their homes. The communicable element of colds can be repeatedly verified, yet often a condition very similar, clinically, may be found to be on an allergic basis. We can rejoice in the increased care with which the common cold is now considered, but as Doctor Meyer points out, we are not yet ready to accept a single etiology.

A most frequent failing in medical science has been the ready acceptance of current theories which have been well publicized. Researches, which allow no sweeping conclusions, have been none the less so interpreted by enthusiasts. All too frequently this has led to overstatement, only checked by the inevitable reaction.

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GEORGE PINESS, M. D. (1136 West Sixth Street, Los Angeles).—The etiology of the common cold is still a mystery to us. Many theories have been advanced, but no one of the many researches carried on to date has been able to establish a specific cause for this most ordinary disease. My own interest in the common cold lies in the point of view that many of the so-called colds are in reality attacks of hay fever, that is, allergic vasomotor rhinitis; and it is not beyond reason to think that the statistics of the incidence of the common cold are vitiated by the frequent occurrence of this manifestation of allergy. Its importance, at least to a certain portion of the population, is certainly as great from the point of view of disability as is the true common cold, and it is not out of place to point out at this time some of its characteristics.

The onset is usually sudden in the early morning hours, but symptoms do not ordinarily persist throughout the day. Characteristically there is a free interval during midday, with a recurrence of symptoms at nightfall. The course is usually much more prolonged than that of the common cold, and of course when seasonal in character it is not likely to be confused with the common cold. The symptoms are usually rhinorrhea, sneezing, nasal obstruction, and itching of

the eyes, nose or throat. Epiphora and burning and smarting of the conjunctivae often accompany the above symptoms and, in fact, may replace them. Unlike the common cold, of course, from our knowledge of the nature of the allergic disturbance a hay fever attack is not contagious, and a fever is rarely observed unless bronchial asthma supervenes, which is not unusual, although it is often overlooked because the only symptom of the involvement of the lower respiratory tract may be in the nature of a bronchitis with cough.

The differential diagnosis between common cold and allergic vasomotor rhinitis is simple, if the obvious symptoms are not dismissed without a thorough history and physical examination. The history, of course, will often show a positive heredity of some type of allergy, or a story of some other allergic disturbance such as urticaria, eczema, or asthma. In addition to this an examination of the mucous membrane of the nose and throat shows a characteristic pallid edematous mucous membrane, often accompanied by mucoid and even polypoid degeneration, and lymphoid hypertrophy in the nasal pharynx.

In calling attention to the frequency with which one meets allergic vasomotor rhinitis in practice, we are in accord with Doctor Meyer's statement that the common cold is not a single disease; and we wish to point out that we can separate allergic vasomotor rhinitis as one of the diseases which contributes to the truth of this statement. Doctor Meyer's discussion of the economic implications resulting from the disability caused by the common cold applies with just as great significance to allergic vasomotor rhinitis, particularly in that extensive group of humans whom we now recognize as allergic.

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WILLIAM J. KERR, M. D. (University of California Hospital, San Francisco).—Doctor Meyer has ably reviewed the prevailing scientific opinion concerning the common cold. The identification of certain clinical states, such as allergic rhinitis, influenza and the common cold, has been difficult, and will remain so until the etiological factors are better known. It should be obvious to anyone that a variety of inciting agents, from without and within the body, may cause a rhinitis resembling a common cold. Since pathogenic bacteria were recognized, attempts have been made to incriminate one or another of the normal inhabitants of the airways, and more recently the ultramicroscopic forms, or filterable viruses, have been suggested as inciting causes alone or in conjunction with bacteria.

Unfortunately, very little attention has been given to the physiological mechanisms of the host, aside from specific immune reactions, during the bacteriological era. If changes in the weather, fatigue, faulty nutrition and other factors making hemostasis difficult are operative, it should be possible to analyze their relationship to the onset of the common cold.

With a view to the study of the circulatory changes occurring in the common cold, Lagen and I have tried to reproduce the common cold so that we could observe the signs during the incubation period, as well as during the various stages of clinical symptoms. We wished to determine in the human being the responses of the heat-regulating mechanisms (skin, kidneys, lungs and respiratory passages) during the progress of the disease.

To date, under carefully controlled environmental conditions, we have been unable to reproduce any symptoms of the common cold by ordinary close exposure of susceptibles to sufferers from the disease, and have not been able to transmit it by direct inoculation of fresh, unfiltered secretions. It is suspected that the filtrates used by some workers are themselves capable of producing a rhinitis, due to the irritating solutions used, which resembles closely a common cold. When we shall have had a sufficiently large series of exposures to satisfy statistical standards, we hope to be able to show that a variety of the disease can be reproduced at will by setting appropriate environmental conditions.

## ROCKY MOUNTAIN SPOTTED FEVER AND ENDEMIC TYPHUS FEVER\*

AS OBSERVED IN CALIFORNIA

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### I. ROCKY MOUNTAIN SPOTTED FEVER

A NUMBER of fevers, of typhus-like character, are distributed over the world. Clinically they are characterized by an abrupt onset, continued fever, a spotted rash, prostration, mental disturbance, and a course of several weeks. There is a serological relationship shown in an ability to give the Felix-Weil reaction, in the production of agglutinins for some strain of *Proteus* X. Such relationship is further suggested by the fact that the so-called Rickettsia bodies have been found associated in the tissues of infected animals and arthropods. They further resemble each other in having some insect as the transmitting vector; as shown both by laboratory experiment and by the finding of infected insects in nature. Further, with the exception of epidemic typhus, they are diseases primarily of rodents, and are transmitted by insects from rodent to rodent, and accidentally from rodent to man. While various of these typhus-like diseases occur in Japan, Australia, eastern Africa, Malaya, Brazil, and other places, these need not be mentioned here. The representatives of this group within the United States include the so-called Rocky Mountain spotted fever, endemic typhus fever, and epidemic typhus. The two first-named are the subjects of this brief consideration.

### ROCKY MOUNTAIN SPOTTED FEVER A MISNOMER

The existence of this disease as a clinical entity has been recognized in this country for half a century. First noted as endemic on the Rocky Mountain plateau, it was given this regional nomenclature. However, the relatively recent discovery of cases in portions of the United States remote from the original endemic area indicates that any such geographical designation is a misnomer.

### ETIOLOGY

The etiological agent of the disease is considered to be either the Rickettsia bodies or associated therewith. These are small, intracellular coccoid or bacillary bodies. They have been cultivated in living tissue; but attempts at culture in media free from living cells have failed. The chief reservoir of the infection exists among wild rodents, among which the disease occurs as a mild epizootic. Squirrels, rabbits, prairie dogs, woodchucks, badgers, and other small animals are susceptible; with ground squirrels and rabbits serving as the most important hosts. The transmitting

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